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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 05/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,837	SEIDAH ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59,60 and 120-127* is/are rejected.

7)☒ Claim(s) *36,37,65 and 67* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 30,31,36,37,40-49,53,56,59,60,65,67,72,73,80-83,95-97,101-103,107-109 and 117-127.

DETAILED ACTION

Response to Amendment

Applicant's cancellations of claims and the amendments to the claims in the Response filed 21 February 2006 have been entered and overcome the rejections and objections of record of claims herein under the first and second paragraphs of 35 U.S.C. § 112, as well as the rejections of claims herein under 35 U.S.C. § 102. The amendments to claims 59 and 60, however, necessitate new grounds of rejection of claims 59, 60 and 120-127 for the reasons set forth below.

Applicant's amendments to the specification in the Response filed 21 February 2006 have been entered and overcome the objections of record to the specification stated in the communication mailed 19 October 2006 for lack of compliance with 37 CFR § 1.821 and the objection of record to the specification for a redundant statement at line 6 of page 39 to "Lys^{137}", but fail to adequately address the objection of record to the specification concerning an incomplete reference at page 31, line 20, to preparation of oligonucleotide primers for cloning a low-density lipoprotein (LDL) receptor cDNA, restated below. The revised Sequence Listing filed 21 February 2006 is ACCEPTED and has been entered, bringing the closure into compliance with 37 CFR § 1.821

Claim Objections

Claims 36, 37, 65, and 67 are objected to because of the following informalities: Claims 36 and 37 recite "[a]n isolated nucleic acid encoding **a** polypeptide (emphasis supplied) defined in", respectively, claims 30 and 31, which statement is inaccurate because neither of claims 30 or 31 describe a set or genus of products and instead define a single product. Similarly, claims 65 and 67 inaccurately recite "[a] composition comprising **a** polypeptide (emphasis supplied) defined in", respectively, claims 30 and 31, where neither of claims 30 or 31 describe a set or genus of products and instead

define a single product. Claim 67 unnecessarily and redundantly adds "of a SKI-1" after "a polypeptide". Appropriate correction, e.g., replacing the indefinite article, "a", before the word "polypeptide" in each of claims 36, 37, 65, and 67 with the definite article, "the", and removing the superfluous recitation "of a SKI-1" from claim 67, is required.

Specification

The amendment filed 21 February 2006 is objected to under 35 U.S.C. § 132(a) because it introduces new matter into the disclosure. 35 U.S.C. § 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The amendatory statement at page 7, line 12, of the Response filed 21 February 2006 adds new matter to the paragraph beginning page 31, line 7, of the specification which is a parenthetical statement, "(Data not shown)". The new matter cannot correct the misleading reference to oligonucleotide primers for cloning a cDNA that specifies a low-density lipoprotein (LDL). Both the added parenthetical statement and the reference to the LDL receptor must be deleted to overcome the objection of record. As noted at page 4 of the communication mailed 19 October 2006, such deletion does not constitute new matter because the words "LDL receptor" do not corroborate any other material aspect of the disclosure.

The amendments to claims 59 and 60 filed 21 February 2006 are also objected to under 35 U.S.C. § 132(a) because they introduce new matter into the disclosure. 35 U.S.C. § 132(a) states that no amendment, and this includes claim amendments, shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The phrases "and with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP)" that are added to both of claims 59 and 60. While this "proviso", a negative limitation, had been

present in the originally filed claims 17 and 18 drawn to methods for substrate cleavage and protein or peptide production, it was not present in the originally filed claims 28, 30 and 31 that were drawn to methods now described by the pending claims 59 and 60, i.e., "screening [for] a subtilisin-kexin isoenzyme named SKI-1" "monitoring the activity of a subtilisin-kexin isoenzyme named SKI-1". Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59, 60, 120-127 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) 59 and 60 contain subject matter, specifically, the phrases "and with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP)", which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 120-127 are included in this rejection because they depend from claims 59 and 60 but embrace the recitation of the new matter.

Claims 59, 60, 120-127 are also rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This new ground of rejection is necessitated by Applicant's Amendment filed 21 February 2006. The specification fails to exemplify or describe the practice of methods of screening and methods of monitoring the proteolytic activity of the SKI-1 protease having the amino acid sequence of SEQ ID NO:6 with a generic peptide of SEQ IDs

NOs:7, 9, or 11 where the use of such generic peptides cannot have permitted the differentiation of the proteolytic activity of the SKI-1 protease from the proteolytic activity of another protease. The rejected claims reach methods of screening and/or monitoring generic proteolytic activity where neither the claims nor the specification describe how the generic peptide substrates are cleaved only by the SKI-1 protease and not another protease. This is exemplified by the failure of the specification to disclose the isolation of a SKI-1 protease having the amino acid sequence of SEQ ID NO:6, or even the protease of claim 30 from the supernatant of cell culture and its subsequent introduction into an assay buffer for measurement of protease activity in the absence of other proteases. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes neither the relevant identifying characteristics of a peptide recited in the amended claims 59 and 60 that permit its cleavage to distinguish SKI-1 protease activity from that of another protease or the relevant identifying characteristics of an assay wherein SKI-1 alone is present that assure that its proteolytic activity is screened or monitored. The specification's treatment of the claimed subject matter, even the disclosures at page 35, lines 19-23 and of Figures 23 and 24, are considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure, or other properties, of the peptide substrates that can distinguish SKI-1 proteolytic activity from a generic proteolytic activity.

Claims 59, 60, 120-122 and 124-126 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for methods of assaying generic endoproteolytic activity, does not reasonably provide enablement for methods of specifically differentiating the proteolytic activity of the disclosed SKI-1 protease from the endoproteolytic activity of other proteases. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to practice a method of the invention commensurate in scope with these claims.

This new ground of rejection is necessitated by Applicant's Amendment filed 21 February 2006. Claims 59 and 60 contemplate the practice of methods intended to distinguish SKI-1 proteolytic activity from the generic proteolytic activity of other proteases but the specification fails to teach the conditions under which this can occur and the peptides recited in claims 59 and 60 are not disclosed to be specifically cleaved by SKI-1 and not other proteases. It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (discussing eight factors relevant to an analysis of enablement). Applying the factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for differentiating SKI-1 proteolytic activity from the proteolytic activity of other proteases using the peptide sequence of SEQ IDs NOs:7, 9 and 11,

b) the specification lacks working examples wherein SKI-1 proteolytic activity is differentiated from the proteolytic activity of other proteases using the peptide sequence of SEQ IDs NOs:7, 9 and 11,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where the peptide sequence of SEQ IDs NOs:7, 9 and 11 have not been shown to differentiated the proteolytic activity of any particular protease from the proteolytic activity of other proteases.

Thus the scope of methods of screening and monitoring embraced by the claims is unsupported by the present specification even if taken in combination with teachings available in the prior art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that

form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 59, 60, 120-122 and 124-126 are rejected under 35 U.S.C. § 102(e) as being anticipated by Brown et al., of record.

This new ground of rejection is necessitated by Applicant's Amendment filed 21 February 2006. Because the negative limitations added by the claim amendments are new matter and cannot be accorded any weight in construing claims 59 and 60, the methods of detectable cleavage of sterol receptor element binding proteins practiced by Brown et al., i.e., cleaving a SKI-1/Site-1 convertase substrate, anticipates the subject matters of claims 59, 60, 120-122 and 124-126 where the peptides of SEQ IDs NOs:7 and 8 are indistinguishable from an SREBP sequence cleaved by the truncated SKI-1/Site-1 convertase of Brown et al.

Conclusion

While claims 36, 37, 65, and 67 are subject to an objection above, claims 30, 31, 36, 37, 40-49, 53, 56, 65, 67, 72, 73, 80-83, 95-97, 101-103, 107-109, and 117-119, are allowable over the prior art of record, essentially for the reasons set forth at pages 7 and 8 of the communication mailed 19 October 2005.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
5 May 2006

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER